REMARKS

Claims 1, 29, 32 and 49-63 are pending. Claims 44-48 were canceled without prejudice or disclaimer as drawn to non-elected inventions and new claims 49-63 have been added. Claims 1, 4, 29 and 32 have been amended herein to more clearly define the invention. Support for the amendments to claims 1 and 4 can be found in the specification as filed, *e.g.*, page 43, lines 2-4; page 60, lines 14-17; and Table 34. Support for new claims 49-63 can be found in claims 1-4, 29 and 32 as originally filed. No new matter has been added by these amendments.

Information Disclosure Statement

The Examiner has indicated that the form 1449 for the Information Disclosure Statement filed July 9, 2001 is missing from the file. In response, Applicants note that a copy of the form 1449 in question is provided herewith.

Rejections under 35 USC 101

Claims 1-4, 29 and 32 are rejected for lack of utility. Claims 2-4 have been canceled herein. This rejection is therefore moot as it applies to these claims. The rejection is traversed as applied to the remaining claims as amended herein.

The Examiner alleges that the application does not disclose a specific biological role for NOV11 or its specific link to a disease, pathology, metabolic state or developmental state. Further, the Examiner asserts SEQ ID NO:22 has not been shown to be associated with any disease or conditions. Therefore, according to the Examiner, the specification does not disclose a credible, substantial and specific use for the claimed protein of SEQ ID NO:22. Applicants traverse for the reasons described below.

The requirements for satisfying the utility requirement are explained in the Manual of Patent Examination Practice (MPEP) 8th Edition, which states that only one credible assertion of specific and substantial utility, need be specified for an invention:

> Specific Utility
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> A "specific utility" is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention. Office personnel should distinguish between situations where an applicant has disclosed a specific use for or application of the invention and situations where

> the applicant merely indicates that the invention may prove useful without identifying with specificity why it is considered useful. For example, indicating that a compound may be useful in treating unspecified disorders, or that the compound has "useful biological" properties, would not be sufficient to define a specific utility for the compound. Similarly, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be *specific* in the absence of a disclosure of a specific DNA target. A general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed. Contrast the situation where an applicant discloses a specific biological activity and reasonably correlates that activity to a disease condition. Assertions falling within the latter category are sufficient to identify a specific utility for the invention. Assertions that fall in the former category are insufficient to define a specific utility for the invention, especially if the assertion takes the form of a general statement that makes it clear that a "useful" invention may arise from what has been disclosed by the applicant. *Knapp v. Anderson*, 477 F.2d 588, 177 USPQ 688 (CCPA 1973).
>
> Substantial Utility
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> A "substantial utility" defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. For example, both a therapeutic method of treating a known or newly discovered disease and an assay method for identifying compounds that themselves have a "substantial utility" define a "real world" context of use. An assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would also define a "real world" context of use in identifying potential candidates for preventive measures or further monitoring. Section 2107.01

Applicants submit that at least one substantial and specific utility exists for the claimed invention and is readily apparent based on the teachings of the specification. The pending claims are drawn to a polypeptide encoding SEQ ID NO:22. The specification explains that this polypeptide corresponds to the polypeptide encoded by clone CG54656-05 (*see* Table 1 at page 5). Applicants enclose herewith a Declaration from Dr. Valerie Gerlach stating that the polypeptide of SEQ ID NO: 22 can be used to diagnose a specific panoply of breast cancers and the metastatic progression of breast cancer, in addition to its use in determining the developmental stage of the brain in an individual, and thus has a specific and substantial utility. Applicant also encloses herewith an Appendix disclosing the results of substantiating studies performed by Dr. Gerlach. Applicants respectfully assert that the claimed polypeptide of SEQ ID

NO:22 is specifically overexpressed in breast cancer and metastatic breast cancer, and is useful, *inter alia*, as a marker (diagnostic indicator) for breast cancer, thereby demonstrating a "real world" use and patentable utility (*See,* Gerlach Declaration, paragraph 7 and Appendix, Table 2, attached hereto). Applicants further assert that the claimed polypeptide of SEQ ID NO:22 is specifically overexpressed in fetal brain, and is useful, *inter alia*, as a marker (diagnostic indicator) for neurological development, thereby demonstrating a second "real world" use and patentable utility (*See,* Gerlach Declaration, paragraph 6 and Appendix, Table 1, attached hereto).

In the Appendix, the tables depict the scaled results of quantitative gene expression analyses performed using nucleic acids having the sequence of SEQ ID NO:21, which encodes for the polypeptide of SEQ ID NO:22, with gene-specific primers that measure the relative SEQ ID NO:21 expression levels in normal cells or tissues, or developmentally staged tissue samples. The Relative Expression Score for each sample indicates the relative quantity of a SEQ ID NO:13 transcript, with 0.0 indicating no detectable expression and 100.00 indicating highest detectable expression level.

The Examiner states that Applicants "do not provide any specific link between the protein of the invention and any disease, pathology, metabolic state or developmental state." (Office Action, page 3). In response, Applicants assert that the nucleic acid encoding the polypeptide of SEQ ID NO: 22 has been correlated with specific proliferative diseases, including metastatic breast cancer (*See* Gerlach Declaration, paragraph 7 and Appendix, Table 2). Additionally, Applicants have demonstrated that the nucleic acid encoding the polypeptide of SEQ ID NO: 22 is specifically overexpressed in fetal brain tissue versus adult brain tissue. (*See* Gerlach Declaration, paragraph 6 and Appendix, Table 1). Therefore, Applicants have disclosed a correlation between breast cancer and an altered level of the nucleic acid encoding the polypeptide of SEQ ID NO: 22, and have demonstrated that the nucleic acid encoding the polypeptide of SEQ ID NO: 22 is specifically overexpressed in proliferating, fetal brain tissue. The skilled artisan would recognize that the methods described in the Appendix are useful in distinguishing between breast cancer, particularly metastatic breast cancer, and normal tissue. For these reasons, Applicants assert that at least one substantial, specific, and credible utility exists for the polypeptide of SEQ ID NO:22, that is to distinguish between breast cancer and

normal tissue. Applicants thus respectfully request withdrawal of the rejection under 35 U.S.C. §101.

Rejections under 35 USC 112, first paragraph

Lack of Utility

Claims 1-4, 29 and 32 are rejected under 35 USC §112, first paragraph. Specifically, the Examiner notes that the claimed invention is not supported by a specific and substantial asserted utility or a well-established utility. Thus, one skilled in the art would not know how to use the invention. Claims 2-4 have been canceled herein. This rejection is therefore moot as it applies to these claims. Applicants have explained above how the invention claimed has patentable utility. For the same reasons, Applicants also submit they have taught how to use the claimed invention.

Lack of Enablement

The Examiner asserts that "claims to variants having 15% difference in sequence to SEQ ID NO: 22, or to fragments of SEQ ID NO: 22 or its variants" are not enabled. (See Office Action, page 4). In response, Applicants have amended claim 1 herein to recite the phrase "no more than one of the amino acid residues in the sequence are so changed" (emphasis added) instead of "no more than 15% of the amino acid residues," in regards to the claimed variants of SEQ ID NO: 22 or amino acids 48-353 of SEQ ID NO: 22. Applicants note that the specification at Table 34 discloses a polypeptide (SEQ ID NO: 60) that varies from SEQ ID NO: 22 (amino acids 1-350) at a single position. Applicants further note that this single amino acid variant of SEQ ID NO: 22 can be generated by a single A to G substitution at nucleotide 386 of SEQ ID NO: 21, the sequence encoding the polypeptide of SEQ ID NO:22. Therefore, new claims 51 and 60, which recite, in part, that "the variant is the translation of a single nucleotide polymorphism," are fully enabled by the as-filed specification.

Regarding claims 29 and 32, the Examiner asserts that "pharmaceutical compositions ...are not enabled, as no pharmaceutical function has been provided for the protein." Applicants note that claims 29 and 32 have been amended herein to delete the term "pharmaceutical." Therefore, the rejection of claims 1-4, 29 and 32 has been overcome and should be withdrawn.

Rejection Under 35 USC § 102(b)

Claims 1-4, 29 and 32 have been rejected under 35 USC § 102(b) as anticipated by U.S. Patents 5,652,133 ("Murphy") and 5,707,815 ("Charo"). Claims 2-4 have been canceled herein. This rejection is therefore moot as it applies to these claims. The Examiner states that "Murphy discloses a MIP1α/RANTES receptor of SEQ ID NO: 2, which comprises a fragment of 6 contiguous amino acids identical to a fragment of SEQ ID NO: 22, which meets the limitation of claim 1(e)." The Examiner further states that "Charo discloses a human chemokine receptor of SEQ ID NO: 5, which comprises a fragment of 6 contiguous amino acids identical to a fragment of SEQ ID NO: 22, which meets the limitation of claim 1(e). (See Office Action, page 6).

Applicants have amended claim 1 herein to delete 1(e). Murphy and Charo do not teach or suggest the amino acid sequence of SEQ ID NO: 22 or single amino acid variant thereof, or the polypeptide of amino acids 48-353 of SEQ ID NO: 22 or single amino acid variant thereof, as required by claim 1 as amended herein. Therefore, Applicants contend that claims 1, 29 and 32 are novel in view of Murphy and Charo. Thus, this rejection should be withdrawn.

The Commissioner is hereby authorized to charge any fees that may be due, or credit any overpayment of same, to Deposit Account No. 50-0311, Attorney Reference No. 15966-729 (Cura-229). Should any questions or issues arise concerning this application, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

April 21, 2003

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the claims:

Claims 1, 29 and 32 have been amended and new claims 49-63 have been added as follows:

1. (Twice amended) An isolated polypeptide comprising the [an] amino acid sequence [selected from the group consisting] of [:

a)] amino acids 48-353 [a mature form] of SEQ ID NO: 22[;

b) a variant of a mature form of SEQ ID NO: 22, wherein any amino acid in the mature form is changed to a different amino acid, provided that no more than 15% of the amino acid residues in the sequence of the mature form are so changed;

c) the amino acid sequence of SEQ ID NO: 22;

d) a variant of the amino acid sequence of SEQ ID NO: 22 wherein any amino acid specified in the chosen sequence is changed to a different amino acid, provided that no more than 15% of the amino acid residues in the sequence are so changed; and

e) a fragment of any of a) through d)].

2-4. (Canceled).

29. (Amended) A [pharmaceutical] composition comprising the polypeptide of claim 1 and a pharmaceutically acceptable carrier.

44-48. (Canceled).

32. (Amended) A kit comprising in one or more containers, the [pharmaceutical] composition of claim 29.

49. (New) An isolated polypeptide comprising the amino acid sequence of a variant of amino acids 48-353 of SEQ ID NO: 22, wherein any amino acid in amino acids 48-353 of SEQ ID NO: 22 is changed to a different amino acid, provided that no more than one of the amino acid residues in the sequence of amino acids 48-353 of SEQ ID NO: 22 is so changed.

50. (New) The polypeptide of claim 49 that is a naturally occurring allelic variant of amino acids 48-353 of SEQ ID NO: 22.

51. (New) The polypeptide of claim 50, wherein the variant is the translation of a single nucleotide polymorphism.

52. (New) The polypeptide of claim 49 that is a variant polypeptide described therein, wherein any one amino acid specified in the chosen sequence is changed to provide a conservative substitution.

53. (New) A composition comprising the polypeptide of claim 49 and a pharmaceutically acceptable carrier.

54. (New) A kit comprising in one or more containers, the composition of claim 53.

55. (New) An isolated polypeptide comprising the amino acid sequence of SEQ ID NO: 22.

56. (New) A composition comprising the polypeptide of claim 55 and a pharmaceutically acceptable carrier.

57. (New) A kit comprising in one or more containers, the composition of claim 56.

58. (New) An isolated polypeptide comprising the amino acid sequence of a variant of the amino acid sequence of SEQ ID NO: 22 wherein any amino acid specified in the chosen sequence is changed to a different amino acid, provided that no more than one of the amino acid residues in the sequence is so changed.

59. (New) The polypeptide of claim 58 that is a naturally occurring allelic variant of SEQ ID NO: 22.

60. (New) The polypeptide of claim 59, wherein the variant is the translation of a single nucleotide polymorphism.

61. (New) The polypeptide of claim 59 that is a variant polypeptide described therein, wherein any one amino acid specified in the chosen sequence is changed to provide a conservative substitution.

62. (New) A composition comprising the polypeptide of claim 58 and a pharmaceutically acceptable carrier.

63. (New) A kit comprising in one or more containers, the composition of claim 62.